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Environmental Protection Agency

Agency Policy to Premanufacture Testing of New Chemical Substances and Announcement of Rescheduled Meeting and Extension of Comment on Certain Environmental Test Standards

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 720

[OPTS 50024; TSH-FRL 1720-1]

New Chemical Substances; Premanufacture Testing Policy

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule related notice.

SUMMARY: This document announces existing Agency policy concerning an approach to premanufacture testing of new chemical substances. It identifies types of test data concerning physical and chemical properties and health and environmental effects which the Agency recommends be developed by manufacturers planning to manufacture a new chemical substance. This document also identifies test protocols which the Agency recommends be utilized to develop these data. The data elements identified here are those under consideration by the Organization for Economic Cooperation and Development (OECD) as recommended "Minimum Pre-market Data" (MPD) for premarket assessment in the OECD member nations.

FOR FURTHER INFORMATION CONTACT: John B. Ritch, Director, Industry Assistance Office (TS-799), Office of Pesticides and Toxic Substances, Environmental Protection Agency, Rm E-229, 401 M St. SW, Washington, D.C. 20460, Toll free: (800-424-9065), In Washington, D.C.: (202-544-1404).

SUPPLEMENTARY INFORMATION:

I. Introduction

The Toxic Substances Control Act (TSCA), 15 U.S.C. 2601 *et seq.*, establishes a national policy that "adequate data should be developed with respect to the effect of chemical substances and mixtures on health and the environment and that the development of such data should be the responsibility of those who manufacture and those who process such chemical substances and mixtures" (sec. 2(b)(1)). TSCA section 5 establishes a premanufacture notification program and requires the submission of health and environmental effects test data which are in the possession or control of the intended manufacturer or processor of new chemical substances. However, TSCA does not establish a requirement that premanufacture testing be performed on all new chemical substances.

To encourage the voluntary development of premanufacture health and environmental effects test data, EPA has devoted extensive attention to development of a premanufacture testing policy in both national and international forums. EPA reached concensus on such testing within the framework of the Organization for Economic Cooperation and Development (OECD), an international organization of twenty-four nations that includes the major chemical producing nations of the non-communist world. The Agency has considered numerous approaches to premanufacture testing and has solicited and reviewed public comments on both policy and technical aspects of such testing. This document describes the Agency's premanufacture testing policy. It describes a base set of data that the Agency recommends as a starting point for premanufacture testing; and it calls for flexibility and the exercise of professional judgment in utilization of the base set. A number of test protocols are recommended for use in developing the base set data.

II. Background

Under section 5 of the Toxic Substances Control Act (TSCA), 15 U.S.C. section 2604, any person who intends to manufacture or import a new chemical substance for commercial purposes in the United States must submit notice to the Environmental Protection Agency (EPA) at least ninety days before he commences manufacture or import.

Section 3(9) defines a "new chemical substance" as any chemical substance which is not included on the list, or "inventory," of existing chemical substances compiled by EPA under section 8(b). Notices of availability of the Inventory were published in the **Federal Register** of May 15, 1979 (44 FR 28558) and revised on July 29, 1980 (45 FR 50544). As required by section 5, the requirement for premanufacture notification became effective thirty days later on July 1, 1979.

Section 5(d)(1) of the Act defines the contents of a premanufacture notice. It requires the manufacturer to report certain information described in section 8(a)(2), e.g., chemical identity, uses, and exposure data. In addition, section 5(d)(1) requires the submission of test data, in the possession or control of the person submitting the notice, which are related to the effects on health or the environment from the manufacture, processing, distribution in commerce, use, and disposal of the chemical substance. Section 5 does not require that particular tests be performed on all new chemical substances before submission of premanufacture notices.

EPA proposed premanufacture notification requirements and review procedures published in the **Federal Register** of January 10, 1979 (44 FR 2242), together with a reporting form for submission of the information required by Section 5(d)(1). After consideration of the public comments on this proposal, EPA reproposed the reporting form and certain of the reporting requirements published in the **Federal Register** of October 16, 1979 (44 FR 59764). The proposed form and reporting requirements provide a format for submission of data from health and environmental testing. However, they do not require that particular tests be performed.

EPA issued and requested comments on a discussion of premanufacture testing policy and technical issues published in the **Federal Register** of March 16, 1979 (44 FR 16240). The discussion document noted that EPA was considering publishing voluntary premanufacture testing guidance and presented several approaches to constructing such guidance, including the use of a base set.

Seventy-one public comments were received, most of them from chemical manufacturers and trade associations. Most industry commentors recommended that EPA not publish guidance, while a few commentors expressed the view that testing guidance would be of significant benefit to the premanufacture notice program.

The most common argument against publishing premanufacture testing guidance was that the statute does not expressly authorize EPA to publish such testing guidance and, should EPA publish voluntary testing guidance, the Agency would effectively make its use mandatory by using the guidance as a "checklist" for evaluating data adequacy of premanufacture notices.

The Agency believes that it has the authority to publish a non-binding policy statement under section 5. Moreover, the Agency is convinced that the publication of a non-binding policy statement on premanufacture testing is in the public interest. EPA has received numerous individual informal requests from manufacturers to provide guidance for new chemical testing. This policy statement reflects the present Agency policy concerning appropriate new chemical testing and makes it available to the general public. Until such time as this policy is modifed, the Agency will use the base set of data described herein as the starting point for constructing recommended premanufacture testing programs for purposes of both informal requests for guidance and petitions for such guidance submitted under section 4(g) of TSCA.

In response to the second concern mentioned above, the Agency recognizes that it cannot use testing guidance published under section 5 to establish a *de facto* general testing requirement for new chemicals. Section 5(b)(1)(A) provides the mechanism for establishing testing requirements for certain new chemicals. Under section 5(b)(1)(A), a manufacturer of a new chemical subject to a section 4 test rule must submit the test data specified in the rule as part of the premanufacture notice required by section 5.

EPA is exploring ways to apply section 4 test rules to categories of chemical substances as authorized by section 26(c). Once category test rules are in effect, a new chemical substance which is a member of the defined category will be subject to the testing requirements as provided by section 5(b)(1)(A).

Another frequent comment was that, if EPA does recommend a base set, there should be flexibility in its application; i.e., that the manufacturer should retain discretion to modify it to suit various situations that may arise. These commentators stated that a "rigid" base set would preclude scientific discretion to tailor chemical testing to particular chemicals and production and use patterns. The Agency agrees with this comment. The policy calls for use of the base set as a starting point for testing but recognizes that particular circumstances of chemical characteristics and production/use patterns may justify deletion, substitution, or addition of data components. Either more or less testing than reflected by the base set of data may result. The Agency requests that companies which utilize the recommended base set to formulate their testing program for a new chemical explain deletions from or substitutions in the recommended base set.

The premanufacture testing policy contains two basic elements: (1) a base set of data which EPA recommends be developed by manufacturers and (2) recommended test protocols for developing the data. Both elements incorporate the results of international testing harmonization efforts of the Organization for Economic Cooperation and Development (OECD). EPA has been an active participant in this work for the past three years. Harmonization of chemical testing among nations is necessary to improve national controls, to efficiently utilize scarce resources, and to avoid unnecessary barriers to international trade. For these reasons, the development of consistent data requirements and testing methods was identified as a priority issue at the international level by the OECD in 1977.

The efforts to reach agreement on chemical testing have proceeded under tha aegis of the Chemicals Group of the OECD. Five expert groups, each under the leadership of individual member countries, were mandated to prepare, by the end of 1979, "state of the art" reports on mutally agreed, scientifically sound test methods for developing data for the prediction of chemical risk. These groups and lead countries were:

Group and Country

Physical/Chemical Properties—Federal Republic of Germany
Ecotoxicology—Netherlands
Degredation-accumulation A Japan, Federal Republic of Germany
Long-term Toxicology—United States
Short-term Toxicology—United Kingdom

A sixth expert group under the leadership of Sweden, called the Step Systems Group, considered the concept of step-sequence (tiered) testing systems. Based in part on the work of the other expert groups, the Step Systems Group was mandated to develop a step sequence testing scheme, including a recommended minimum premarket data set, for use by member countries in the assessment of new chemical substances.

Approximately 350 government and industry experts from all over the world have participated directly in the work of these expert groups. U.S. participants from government and industry numbered about twenty-five. In addition, the work of these groups has been formally reviewed and commented upon by the major international business and trade union organizations, the OECD Business and Industry Advisory Committee (BIAC), the OECD Trade Union Advisory Committee (TUAC), and a number of U.S. chemical manufacturers, trade associations, and environmental organizations.

With minor exceptions, the final reports of the five expert groups on testing were completed by the end of 1979 and all are complete at this time. These groups developed approximately 44 separate test methods (called "test guidelines" in OECD documents). Some of these test methods are considered final, while others are still undergoing inter-laboratory validation. In addition, most of the final reports from these groups identified particular tests which are appropriate for providing data for a premarkct assessment.

Based in part on the work of these groups, the Expert Group on Step Systems produced a preliminary final report which contained a recommended premarket base set of data called the "Minimum Premarket Data" set (MPD).

The reports of all six expert groups were made available for public comment in the U.S. in April, 1980. (See "Organization for Economic Cooperation and Development (OECD) Chemicals Program; Final Reports on Testing Guidelines; Notice of Availability, "published in the **Federal Register** of April 17, 1980 (45 FR 26129).) Thrity-one comments were received. Commentators were divided on the Step Systems Group report, which recommended flexible application of the MPD. Three commentators supported the MPD, and one recommended against its use by EPA. Several other commentators expressed reservation about the use of the MPD and stressed the need for flexibility in its application.

Most commentators felt that the expert group reports containing test protocols were of high quality. Several commentators stressed the need for some flexibility in the recommended OECD test procedures, and there were numerous technical comments on the procedures themselves. These comments were considered by EPA and the U.S. delegation to the High Level Meeting of the OECD Chemicals Group, which took place in May, 1980.

Environmental ministers and senior officials from other concerned regulatory agencies of the OECD member nations met in May, 1980, to review the work of the expert groups and to make recommendations to the OECD Council concerning disposition of various work products. At that meeting, the participants endorsed the work of the expert groups and recommended that the final test methods be adopted and that draft methods be made final. In addition, they endorsed the minimum premarket set of data developed by the Step Systems Group and recommended that it and the various test guidelines be provisionally applied in member countries pending approval by the OECD Council. In December, 1980, the Environment Committee of the OECD also endorsed the MPD and test guidelines and recommended that the OECD Council publish both as a Council decision, which would make them binding on member nations. EPA anticipates that the OECD Council will issue a decision on the MPD and test guidelines early next year.

The base set of data which EPA is recommending herein is identical to the MPD developed by the OECD. The term "base set" will be used in this notice to denote the MPD.

It is recognized within the OECD working groups that, although the recommended base set tests are

generally applicable to new chemicals, not all may be applicable in certain circumstances. The OECD working groups also recognize that additional testing beyond the base set may be appropriate for some chemicals, as indicated by base set test results and/or circumstances of use and exposure. Current OECD plans are to develop general "flexibility criteria" to provide guidance concerning deviations from the recommended set of tests. EPA plans to incorporate such flexibility criteria into its premanufacture testing policy as the criteria are developed by the OECD.

The base set is the first step in the step sequence testing scheme that is being developed by the OECD. EPA will continue to participate in efforts to develop the remainder of the step sequence scheme. As further steps are agreed upon in the OECD, EPA plans to modify the premanufacture testing policy stated here accordingly.

In addition to these international testing harmonization efforts, EPA as been active in efforts of the Interagency Regulatory Liaison Group (RLG) to harmonize testing methodologies among the U.S. chemical regulatory agencies. The IRLG is comprised of representatives from the Consumer Product Safety Commission, the Food and Drug Administration, the Occupational Safety and Health Administration, and the Department of Agricultural Food Safety and Quality Service in addition to EPA. The National Toxicology Program (represented by the National Cancer Institute), the Department of Commerce, and the Department of Energy have participated as advisors.

The purpose of the IRLG effort is to develop uniform testing methodologies to provide data for chemical assessment purposes. To date, the IRLG has, after public review, finalized test standards for acute oral toxicity, acute dermal toxicity, acute eye irritation, and teratology. Test standards for a number of other health effects, as well as for envionmental effects and physical chemical properties, are under development. These standards, which will be consistent with the OECD test guidelines, will be published for public comment by the IRLG during the coming months.

III. Policy Statment

EPA recommends that manufacturers of a new chemical substance subject to the premanufacture notification requirements of TSCA utlize the base set of data listed below as a starting point for designing a premanufacture testing program.

A. Recommended Base Set

1. Physical/Chemical Data:

Melting point/melting range
Boiling point/boiling range
Density of liquids and solids
Vapor pressure
Water solubility
Partition coefficient, n-octanol/water
Hydrolysis (as a function of pH)
Spectra (UV and visible)
Soil adsorption/desorption
Dissociation constant
Particle size distribution

2. Acute Toxicity Data:

Actute oral toxicity
Actute dermal toxicity
Actute inhalation toxicity
Skin irritation
Skin sensitization
Eye irritation (for chemicals showing no skin irritation)

3. Repeated Dose Toxicity Data:

14–28 days, repeated dose test(s) using probable routes(s) of human exposure

4. Mutagenicity Data (Screening Tests):

Gene (point) mutation
Chromosome aberrations

5. Ecotoxicity Data:

Acute toxicity, LC_{50} study, fish (96 hour)
Daphnia reproduction study (3 broods)
Growth inhibition study, unicellular alga (4 days)

6. Degradation/Accumulation Data:

Ready Degradability
Bioaccumulation (uptake from medium)

B. Recommended Test Methodologies

EPA recommends that tests to provide the data elements listed above be performed according to methods published by the OECD, the IRLG, or by EPA test standards promulgated under section 4 of TSCA, section 3 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), or other approved EPA methods. In the absence of final test methods from one of these sources, other test methods which are generally accepted among professionals in the particular scientific field would be appropriate.

Sources for TSCA, FIFRA, and IRLG tests will be cited later in this notice. The OECD test guidelines will be published by OECD in early 1981. In addition, EPA plans to make them available from the Industry Assistance Office in the near future. They may be requested by calling the toll free number given earlier in this notice.

C. Modifications

The base set may be modified to suit particular chemicals and production/use patterns. For example, technical considerations may make some tests inapplicable for certain chemicals. Also, in some cases, the results of some physical/chemical properties tests may indicate that certain other tests are unnecessary or inappropriate. In circumstances of very low human exposure or environmental release, a lesser amount of testing may be warranted.

Other considerations may suggest that additional testing should be performed. For example, structure/activity analysis may suggest the need for testing for carcinogenic effects, which are not directly addressed in the base set. Similarly, circumstances of high potential human exposure or environmental release would generally indicate a need for additional testing. For example, in circumstances of repeated human exposure, a 90-day subchronic test and tests for teratogenic and reproductive effects would be recommended.

The screening-level base set data also may indicate the need for follow-up testing. For example, the data may indicate the need for oncogenicity, chronic toxicity, or additional ecological effects tests. EPA is continuing to study the relationship of various "follow-up" tests to the tests in the base set recommended here. In the future, the Agency expects to publish guidance concerning such relationships.

Similarly, particular circumstances may require modification of a test method. In such case, the modification should not reduce the effectivenss or accurracy of the test.

EPA requests persons using the recommended base set data as a starting point for premanufacture testing to explain the scientific rationale for any deletions, substitutions or additions to the base set. EPA also requests persons who modify a recommended test method, or who substitute a different test method, to provide the protocol and a scientific rationale for the change.

IV. Discussion

The recommended base set of data elements is intended to provide information which, in conjunction with required premanufacure information related to use and exposure, will permit an initial assessment of potential risk which a chemical substance may present to health or the environment. The base set of data was constructed with both scientific and economic considerations in mind. Each data element supplies information that is useful for risk assessment, as explained more fully below. Also data elements related to certain important effects, for

example teratogenicity and neurotoxicity, are not included in the base set because relatively inexpensive and reliable (validated) screening tests are not available.

A. Relationships To Section 5(e) Actions

Section 5(e) of TSCA authorizes EPA to prohibit or limit manufacture of a new chemical substance if the Agency does not have sufficient information to conduct a reasoned risk assessment but finds that the chemical may present an unreasonable risk or that it is or will be produced in substantial quantities and either enters or may reasonably be anticipated to enter the environment in substantial quantities or there is or may be significant or substantial human exposure to the substance. EPA will consider all available relevant information in determining whether to initiate a 5(e) action concerning a premanufacture notice. EPA will not automatically initiate 5(e) actions if a manufacturer declines to utilize the recommended base set or deviates from the base set.

B. Test Cost analysis

Since there are no published cost data for OECD test guidelines, EPA requested a contractor (Contract No. 68–01–5864) to develop an appropriate methodology and estimate the cost of these protocols. The methodology and analysis are presented in a separate document entitled *Cost Analysis Methodology and Protocol Estimates: OECD Minimum Premarket Data (MPD) Test Protocols,* January, 1981, which may be obtained from the information contact above. Because so me OECD test guidelines are not currently being used in the United States, the estimated costs shown below should be considered only representative of actual costs. The test costs are not additive since the total cost to a firm will be determined by the testing program devised and followed by that firm for each individual chemical. Because this policy statement establishes voluntary testing guidance rather than regulations, an economic impact analysis is not warranted.

The Agency has initiated a study of the over-all economic impacts of TSCA on the chemical industry. This study will examine changes in research and development programs for new chemicals including changes in testing as well as such effects as impacts on growth, innovation, and international trade. By looking at the impacts of all TSCA regulations (testing, premanufacturing notification, control actions, and reporting requirements), the Agency believes that it will be better able to analyze the economic impact of TSCA.

C. Base Set Data Elelments

The following discussion provides, for each base set data element, an explanation of its utility in performing a risk assessment, references to or sources for the recommended test protocols for each element, and available information on the estimated cost of performing the test according to the protocol.

1. *Physical/chemical properties.* (a) Melting Point/melting range. (1) Contribution to risk assessment. The melting point of a chemical is the temperature at which the solid and liquid forms of the chemical are in equilibrium. Data on melting point/melting range are useful for chemical fate and exposure analysis because they indicate the physical state of a chemical substance at ambient temperatures. This gives an indication of the distribution of the substance in the water, soil, and air. In addition, the melting point is important for identification purposes and, as a measure of purity, can give indication of impurities which may have environmental relevance. Melting point data may also be useful for the design of other tests of the chemical.

(2) Test protocols and estimated cost.
OECD: Estimated cost of test—$100.
IRLG: None.
TSCA, section 4: Proposed—45 FR 77341, § 772.122–2.
FIFRA, section 3: Proposed—43 FR 29710, § 163.61–8(3) and 43 FR 29712 (Appendix).

(b) *Boiling point/boiling range.* (1) Contribution to risk assessment. The boiling point of a liquid is the temperature at which its vapor pressure equals the pressure of its surrounding environment. Data on boiling point/boiling range are useful for chemical fate and exposure analysis because they indicate the physical form of the substance at ambient temperatures. A boiling point near ambient temperatures indicates the possibility of vaporization of the substance, with concommitant possibility of exposure by inhalation. These data are also useful for identification purposes, and may contribute to the design of other tests of the chemical.

(2) Test protocols and estimated cost.
OECD: Estimated cost of test—$50.
IRLG: None.
TSCA, section 4: In preparation
FIFRA, section 3: Proposed—43 FR 29710, § 163.61–8(9) and 43 FR 29712 (Appendix).

(c) *Density of liquids and solids.* (1) Contribution to risk assessment. Density is the mass per unit volume of a chemical substance at a specified temperature. Data on density is useful for assessment of chemical transport and fate because it indicates whether immiscible, low-reactivity chemicals will tend to sink or float when released into water.

(2) Test protocols and estimated cost.
OECD: Estimated cost of test—$50.
IRLG: None.
TSCA, section 4: Proposed—45 FR 77338, § 772.122–1.
FIFRA, section 3: Proposed—43 FR 29710, § 163.61–8(8) and 43 FR 29712 (Appendix).

(d) *Vapor pressure curve.* (1) Contribution to risk assessment. Vapor pressure values indicate the tendency of pure substances to vaporize and thus provide an indication of the relative volatilities of chemical substances. Volatility is an important consideration in assessing chemical fate and potential for exposure, because volatization may lead to dispersal of an uncontained chemical substance over wide areas. Also the vapor pressure can be useful in deciding whether to conduct a photochemical degradation test.

(2) Test protocols and estimated cost.
OECD: Estimated cost of test—$300.
IRLG: None.
TSCA, section 4: Proposed—45 FR 77345, § 772.122–3.
FIFRA, section 3: Proposed—43 FR 29710, § 163.61–8(10) and 43 FR 29712 (Appendix).

(e) *Water solubility.* (1) Contribution to risk assessment. The water solubility of a chemical is an important parameter determining its environmental transport and distribution. In general, highly soluble chemicals are more likely than poorly soluble chemicals to be distributed by the hydrologic cycle. In addition, water solubility can affect adsorption and desorption on soils and volatility from aquatic systems, as well as possible transformation by hydrolysis, photolysis, oxidation, reduction, and biodegradation in water. Also, knowledge of water solubility is needed for the design of most chemical tests and many ecological and health tests. Water solubility also affects uptake by humans and other living organisms.

(2) Test protocols and estimated cost.
OECD Estimated cost of test—$300.
IRLG: None.
TSCA, section 4: In preparation.
FIFRA, section 3: Proposed—43 FR 29710, § 163.61–8(4) and 43 FR. 29712 (Appendix).

(f) *Octanol/water partition coefficient.* (1) Contribution to risk assessment. The octanol/water partition coefficient, P, is the ratio of the equilibrium molar concentrations of a chemical substance in octanol and

water. Accumulation and transport of a chemical substance in a living organism are governed by polarity, water solubility, affinity for fatty tissues, and the nature of potential binding to biological receptors. The octanol/water partition coefficient measures the relative equilibrium distribution of a substance between the fat and water phases of the test system. It therefore serves as an indicator of bioconcentration potential in fatty tissues and of the ability to pass through all membranes. Bioconcentration potential is an important factor in assessing chemical risk. In conjunction with data on chemical persistence, bioconcentration potential may be used to identify chemicals which may be transported via food chains.

(2) Test protocols and testimated cost.
OECD: Estimated cost of test—$250.
IRLG: None.
TSCA, section 4: Proposed—45 FR 77350, § 772.122–4.
FIFRA, section 3: Proposed—43 FR 29710, § 163.61–8(6) and 43 FR 29712 (Appendix).

(g) *Hydrolysis (as a function of pH).* (1) Contribution to risk assessment. Hydrolysis can be an important phenomenon in determining the persistence of a chemical substance in the environment. Chemical substances may undergo hydrolysis and be transformed into new substances with properties different from their precursors. The importance of these transformations of chemcials as dominant pathways in aqueous media can be determined quantititatively from data on hydrolysis rate constants.

(2) Test protocols and estimated cost.
OECD: Estimated cost of test—$250.
IRLG: None.
TSCA, section 4: In preparation.
FIFRA, section 3: Proposed—43 FR 29717, § 163.62–7(b) and 43 FR 29721 (Appendix).

(h) *Spectra (UV and visible).* (1) Contribution to risk assessment. The ultraviolet and visible light absorption spectra of chemical substances in solution are important physical properties that are characteristic of molecular structure. Spectral data can give indications of the wavelenghts at which photochemical degradation of the chemical may occur. Such data are therefore useful for determining the need for further testing of persistence in the atmosphere or aquatic environment.

(2) Test protocols and estimated cost.
OCED: Estimated cost of test—$200.
IRLG: None.
TSCA, section 4: In preparation.
FIFRA, section 3; Proposed—43 FR 29710, § 163.61–7(b)(2) and 43 FR 29712 (Appendix).

(i) *Soil adsorption/desorption.* (1) Contribution to risk assessment. The affinity of a chemical substance for particulate substances is an important factor affecting its environmental movement and ultimate fate. Substances that adsorb tightly to soil particles may be less subject to environmental transport in the gaseous phase or in solution. On the other hand, high adsorptivity to soil particles may increase environmental transport with windblown dust or eroding soil; high adsorptivity may also lead to accumulation of the substance in the soil.

(2) Test requirements and/or protocols and estimated cost.
OECD: Estimated cost of test—$2,000.
IRLG: None.
TSCA, section 4: Proposed—45 FR 77352, § 772.122–5.
FIFRA, section 3: Proposed—43 FR 29716, § 163.62–5(c) and 29719 § 163.62–9(d) and 29721 (Appendix).

(j) *Dissociation constant.* (1) Contribution to risk assessment. The dissociation characteristics of a chemical are important for risk assessment because they govern the form in which the chemical exists. This, in turn, determines its chemical behavior and transport characteristics. Dissociation also affects adsorption onto soil particles and sediments and movement into and out of living cells.

(2) Test protocols and estimated cost.
OECD: Estimated cost of test—$150.
IRLG: None.
TSCA, section 4: In preparation.
FIFRA, section 3: None.

(k) *Particle size distribution.* (1) Contribution to risk assessment. Particle size distribution affects the probability of human inhalation or ingestion of a limited sub-class of particulates as well as the likely point of their deposition in the respiratory tract. It also influences the distribution of a particle in the environment. Accordingly, the data element which describes particle size is important because it identifies potential health hazards arising from human inspiration due to direct exposure and provides information on the transportation and sedimentation of particulates in water and air.

(2) Test protocols and estimated cost.
OECD: Estimated cost of test—$100.
IRLG: None.
TSCA, section 4: In preparation.
FIFRA, section 3: None.

2. *Ecotoxicology.* (a) *Acute toxicity to fish.* (1) Contribution to risk assessment. Data on a chemical's toxicity to fish are important because of the substantial value of commercial and recreational fishing and the essential functional role of fish in aquatic food chains. These studies provide data to determine the median lethal concentration (LC_{50}) of a chemical substance for fish, and permit estimation of the chemical's toxicity to a vertebrate species relative to that of other chemicals. This estimation of relative toxicity contributes to the assignment of priorities for further testing. In addition, acute toxicity tests may provide guidance for subsequent chronic testing.

(2) Test protocols and estimated cost.
OECD: Estimated cost of testing—$1,250 (includes LC_{50}, rangefinding test, and analytical assay).
IRLG: None.
TSCA, section 4: In preparation.
FIFRA, section 3: Proposed—43 FR 29734, § 163.72–1.

(b) *Growth inhibition study, unicellular algae.* (1) Contribution to risk assessment. Testing for inhibition of the growth of algae indicates the extent to which a chemical substance can affect primary producers in lakes, streams, estuaries, and oceans. This testing provides data from which threshold toxicity values can be determined and positioned relative to other chemicals. This study can also generally indicate growth stimulation as well as growth inhibition. Algae are particularly important as test organisms among plants because they constitute the major mechanism for fixation of energy in most aquatic environments.

(2) Test protocols and estimated cost.
OECD: Estimated cost of testing—$1,450 (includes IC_{50}, rangefinding test and analytical assay.)
IRLG: None.
TSCA, section 4: In preparation.
FIFRA, section 3: None.

(c) *Daphnia* reproduction study (3 broods). (1) Contribution to risk assessment. Daphnia provide important data for risk assessment because they are very sensitive to toxic substances and serve in the base set as a representtive of invertebrate species. This life-cycle study permits a more complete evaulation of potential hazard from chronic exposure to a chemical through the different life stages and functions of the organism.

(2) Test protocols and estimated cost.
OECD: Estimated cost of testing—$1,400 (includes reproduction test rangefindings test and analytical assay.)
IRLG: None.
TSCA, section 4: In preparation.
FIFRA, section 3: None.

3. *Degradation/Accumulation.* (a) *ready biodegradability.* (1) contribution to risk assessment. Biodegradation is the predominant mechanism for mass transformation of orgnic compounds in soil and water. Biodegradation data

permits a more realistic prediction of the chemical's environmental concentration, which is essential to an adequate assessment of its risk to the environment.

Biodegradation is also the most important degradative mechanism for organic compounds with respect to extent degradation; photochemical to chemical degradation and other processes usually do not completely mineralize organic substances. The form of a chemical which is most prevalent in the environment is an important aspect of risk. Accordingly, knowledge of the extent of a chemical's potential to biodegrade is necessary to determine the environmental fate of a chemical. It is also essential to assess the risk posed by the chemical to the environment.

Testing for ready biodegradability also contributes to risk assessment by providing a preliminary indication of the test substance's effect on mocroorganisms. Moreover, these data can indicate the potential effects of a new chemical on the microbial population and thus on the effectiveness of a secondary sewage treatment plant.

(2) Test protocols and estimated cost.

OECD: Estimated cost of test—range of $250 to $9,000 (depending on which of several tests is selected).

Note.— The OECD Expert Group on Degradation/Accumulation has identified five candidate tests for assessing "ready biogradability," and has provided guidance for selecting the appropriate test for various types of chemicals.

IRLG: None.

TSCA, section 4: In preparation.

FIFRA, section 3: Proposed—43 FR 29716, § 163.62–7 and 29720 § 163.62–11.

(b) *Bioaccumulation* (uptake from medium). (1) contribution ot risk assessment. The tendency to bioaccumulate enables chemical substance to cause toxic injury and alter ecological processes at concentrations much lower than those predicted from acute and subacute studies. Moreover, it enhances the chemical's ability to affect life far removed from the initial points of entry into the environment. More indirect effects can occur when a chemical which is highly accumulative contaminates organisms like fish to the extent that they are unsafe or undesirable to consumers.

Preliminary screening data is necessary to distinguish chemcial substances with low or moderate bioaccumulative character from those with high bioaccumulative character. This information will be used in conjunction with data on toxicity, transport, and fate of a chemical to assess the risk resulting from the release of that chemical into the environment.

(2) Test protocols and estimated cost.

OECD: There are two OECD base set bioaccumulation tests: bioconcentration in marine organisms (estimated cost $850) and static bioaccumulation in fish (estimated cost $2,000).

IRLG: None.

TSCA, section 4: In preparation.

FIFRA, section 3: 43 FR 29720, § 163.62–11.

4. *Toxicity Studies For Human Health Effects.* (a) *Acute Toxicity: Oral, dermal, and inhalation.* (1) Contribution to risk assessment. Acute toxicity studies must be determined to assess the potential risk of poisoning by a single exposure to a new chemical. These studies provide data to determine the median lethal dose (LD_{50}) of a chemical substance and permit estimation of the toxicity of this substance relative to that of other chemicals. They may also provide data to approximate its mode(s) of action, to determine its specific toxic effect(s) on target organs and functions, and to determine any difference in sensitivity to this substance among species or routes of exposure.

(2) Test protocols and estimated cost.

OECD: Estimated cost of tests—Acute Oral Toxicity $2,000; Acute Dermal Toxicity $2,800; Acute Inhalation Toxicity $3,300.

IRLG: 44 FR 49015 (announces availability of draft guidelines from Industry Assistance Office)

TSCA, section 4: (i) Acute Oral Toxicity-Proposed—44 FR 44066, § 772.112–21; (ii) Acute Dermal Toxicity-Proposed—44 FR 44067, § 772.112–22; (iii) Acute Inhalation Toxicity-Proposed—44 FR 44067, § 772.112–23.

FIFRA, section 3: (i) Acute Oral Toxicity-Proposed—43 FR 37355, § 163.81–1; (ii) Acute Dermal Toxicity-Proposed—43 FR 37356, § 163.81–2; (iii) Acute Inhalation Toxicity-Proposed—43 FR 37357, § 163.81–3.

(b) *Primary dermal irritation/corrosion.* (1) Contribution to risk assessment. Data from a primary dermal irritation study indicate the capacity of a chemical to cause irritation and/or corrosion effects on the skin of laboratory animals. This evaluation can be used to guide health and safety practices for the handling of a chemical substance.

(2) Test protocols and estimated cost.

OECD: Estimated cost of test—$700.

IRLG: None.

TSCA, section 4: Proposed—44 FR 44071, § 772.112–25.

FIFRA, section 3: Proposed—43 FR 37360, § 163.81–5.

(c) *Primary eye irritation/corrosion.* (1) Contribution to risk assessment. Data from a primary eye irritation study indicate the capacity of a substance to produce injury to the eye and associated mucus membranes. Evaluation of this potential hazard can be used to guide health and safety practices for the handling of a chemical substance.

(2) Test protocols and estimated cost.

OECD: Estimated cost of test—$450.

IRLG: 44 FR 49015.

TSCA, section 4: Proposed—44 44070, § 772.112–24.

FIFRA, section 3: Proposed—43 FR 37359, § 163.81–4.

(d) *Skin sensitization.* (1) Contribution to risk assessment. Data from dermal sensitization studies indicate the capacity of a chemical to induce a state of delayed contact sensitization when it comes in contact with the skin of laboratory animals. The evaluation of a chemical for potential skin sensitizing hazard can be used to guide health and safety practices for the handling of a chemical substance.

(2) Test protocols and estimated cost.

OECD: Available in 1981. Estimated cost of test—range of $3,200 to $6,700 (depending on which method is selected)

IRLG: None.

TSCA, section 4: Proposed—44 FR 44071, § 772.112–26.

FIFRA, section 3: Proposed—43 FR 37361, § 163.81–6.

(a) *14–28 day repeated dose.* (1) Contribution to risk assessment. Repeated dose toxicity studies are performed to determine dose-respone relationships and major organ toxicity associated with repeated exposure to a test substance. Repeated dose information is also of fundamental importance in cost effectively designing expensive subchronic or chronic toxicity studies with much longer exposure periods.

(2) Test protocols and estimated cost.

OECD: Available in 1981.

Estimated cost of test—$10,200–12,800.

IRLG: None.

TSCA, section 4: Proposed—44 FR 44072, § 772.112–31.

Note.—The TSCA protocol calls for a minimum 90-day study on a rodent and non-rodent species.

FIFRA, section 3: Proposed—43 FR 37363, § 163.82.

Note.—The FIFRA protocol calls for a minimum 90-day study of a rodent and non-rodent species.

(f) *Mutagenicity.* (1) Contribution to risk assessment. Data from mutagenicity studies may indicate the capacity of a substance to produce alterations (mutation) in the genetic materials of a

cell either at the gene or chromosome level. Such mutations may result in teratogenic or carcinogenic effects in exposed persons, as well as mutagenic effects that are transmitted to future generations. Since some chemicals induce only one genetic alteration, studies for both gene (point) mutations and chromosomal aberrations are needed in the basic screening step. The preferred test for gene mutations is the *S. typhimurium* reversal mutation assay (Ames test). The *E. coli* WP2 reverse mutation assay may be substituted if this system is likely to be more sensitive to the test chemical. While an *in vitro* mammalian cytogenetics test is preferred in testing for chromosome aberrations, an *in vivo* mammalian cytogenetics test may be substituted where a scientific rationale exists.

(2) Test protocols and estimated cost.

OECD: Estimated cost of tests. (i) *Gene Mutations-S. typhimurium* Reverse Mutation Assay—$1,000; *E. coli* WP2 Reverse Mutation Assay—$350. (ii) *Chromosome Aberrations-In vitro* mammalian cytogenetics test $3,000; *In vivo* mammalian bone marrow cytogenetics test; $13,000 Micronucleus test—$2,000.

IRLG: None.

TSCA, Section 4: Proposed—44 FR 44054, § 772.114–1—772.114–4.

FIFRA, Section 3: Proposed—43 FR 37388, § 163.84–1—163.84–4.

Dated: January 19, 1981.

(15 U.S.C. 2601 et seq.)

Douglas M. Costle,

Administrator.

[FR Doc. 81–2851 Filed 1–26–81; 8:45 am]

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40 CFR Part 772

[OPTS–46007A; TSH FRL 1593–3–1594–4; TSH–FRL 1720–1a]

Environmental Test Standards: Clarification of Policy; Extension of Time for Comment and Rescheduled Meeting

AGENCY: Environmental Protection Agency (EPA).

ACTION: Extension of time for comment.

SUMMARY: This notice extends the comment period and reschedules the related meeting, open to the public, to receive oral comment for the Agency's proposal of certain environmental test standards published in the Federal Register on November 21, 1980 at (45 FR 77332). This notice also gives a clarification of policy respecting that proposal's preamble discussion of these standards' relationship to international guidelines, particularly those being developed through the Organization for Economic Cooperation and Development (OECD).

DATES: Written comments should be submitted on or before Monday, March 16, 1981. The opportunity to present oral comments in an open meeting has been rescheduled to Tuesday, March 31, 1981, 1:00–5:00 p.m. The previously announced meeting for February 10th is hereby canceled. See below for further details on this open meeting.

ADDRESSES: Written comments should bear the EPA document control number (OPTS–46007A) and should be submitted to: Document Control Officer (TS–793), Management Support Division, Office of Pesticides and Toxic Substances (OPTS), Environmental Protection Agency, Room E447, 401 M St., SW, Washington, D.C. 20460, (202–755–8050).

See Supplementary Information, Extension of Time for Comment for location of the open meeting.

FOR FURTHER INFORMATION CONTACT: John B. Ritch, Jr., Director, Industry Assistance Office (TS–799), Office of Pesticides and Toxic Substances, Environmental Protection Agency, Room E427, 401 M St., SW, Washington, D.C. 20460, Toll free: (800–424–9065); in Washington, D.C.: (202–554–1404).

SUPPLEMENTARY INFORMATION:

I. Background

The Agency is proposing a series of generic standards for development of test data to have available for incorporation in specific chemical testing rules as they are issued under section 4 of the Toxic Substances Control Act (TSCA). The authority for these proposals is TSCA, Pub. L. 94–469; 90 Stat. 2006; 15 U.S.C. 2603. Previously published proposals covered the development of data on chronic health effects and Good Laboratory Practices for health effects (May 9, 1979, 44 FR 27334), and also on acute and subchronic toxicity, mutagenic, teratogenic and reproductive effects and metabolism studies (July 26, 1979, 44 FR 44054). On November 21, 1980 (45 FR 77332) the Agency proposed standards for development of test data on certain physical and chemical characteristics of substances and Good Laboratory Practices related to environmental effects testing. The notice covered testing for Density/Relative Density, Melting Temperature, Vapor Pressure, Octanol/Water Partition Coefficient and Soil Thin Layer Chromatography. In the future the Agency will be proposing additional test standards for neurobehavioral toxicity, other physical, chemical and environmental persistence characteristics and various ecological effects.

In the preamble to the November 21st proposal (45 FR 77335) the Agency discussed the relationship of TSCA test standards to interagency and international test guidelines. Since then, the Agency has been requested to clarify this relationship, in particular with respect to its activities within the framework of the Organization for Economic Cooperation and Development (OECD). The clarification of policy below addresses this concern.

II. Clarification of Policy: Relationship to International Guidelines

In proposing these requirements, EPA recognized its obligations under Title IV of the Trade Agreements Act of 1979 (Pub. L. 96–39). That law provides the legal framework for implementing trade agreements entered into by the United States. Title IV (the Standards Code), by setting forth principles and procedures for Federal agencies, including EPA, to follow in rulemaking, aims at preventing the creation of unnecessary technical barriers to foreign trade.

As stated in section 401, the Standards Code is not intended to prevent Federal agencies from making rules or setting standards affecting international trade, for example, in chemical products, if such measures have as a demonstrable purpose the achievement of a legitimate domestic objective, such as protecting health, safety or the environment within the United States, and do not operate to exclude imported products which fully meet the objectives of such measures. Title IV states, however, that agencies involved in such rulemaking shall consider the adoption of existing international standards, if they are appropriate, and shall ensure that imported products are treated no less favorably than like domestic or other imported products.

As noted in the earlier Federal Register notice, the U.S. EPA has been a full and regular partner in extensive international consultations and negotiations in the OECD during the development of its chemical testing and other requirements under TSCA. The Agency places a high priority on these activities because of benefits both for international chemical trade and for more effective health and environmental protection.

U.S. experts, along with those of other OECD member states, have worked since 1977 to develop agreed chemical testing guidelines and good laboratory practices, as well as an agreed set of data that should be developed for new chemicals prior to marketing. The

United States strongly endorsed the work of the expert groups at a meeting of high level national regulatory officials in May 1980 and firmly committed the United States to domestic implementation.

Therefore, the policy of the United States with respect to the current proposal is to pursue consistency in its test standards with the OECD Test Guidelines. They will have the same basic requirements, so that data developed according to either EPA or OECD procedures with respect to those requirements should satisfy EPA needs.

A concerted effort will be made to incorporate OECD wording into EPA standards/guidelines; however, where EPA language provides a substantial improvement or is necessary to comply with a U.S. statutory or judicial requirement, it can be used. Additions to, or deletions from, the OECD guidelines will be strickly limited and a rationale provided in such cases. Additions should generally be limited to suggested or preferred criteria or to explanatory phrases (rather than required) such that the basic requirements cannot be construed as being different.

III. Extension of Time for Comment

In the November 21st notice, a deadline of January 21, 1981 was set for receiving written comments, and an opportunity to present oral comment was offered on February 10, 1981. Today's notice extends the time for filing written comments until Monday, March 16, 1981, cancels the February 10th meeting and announces a new opportunity to present oral comment in an open meeting on March 31, 1981.

Several foreign governments have indicated a desire to comment on these proposed test standards and a difficulty in doing so before the deadline set for written comment. In addition, interested parties in the U.S. have requested an extension of the comment period. therefore, the Agency is granting an extension of the time for comment. Directions for filing written comment are given under ADDRESSES above.

The open meeting will be held from 1:00 p.m. to 5:00 p.m., Tuesday, March 31, 1981, in Room M3906, Waterside Mall, U.S.E.P.A. Headquarters, 401 M Street, S.W., Washington, D.C. 20460. The opportunity to present oral comment is granted to persons having some information, interpretation or argument on alternatives that is not duplicative of their written commentary and is more easily communicated in an oral exchange than in writing. Persons wishing to make presentations should request time by contacting the Industry Assistance Office by telephone (800-242-9065 or, in Washington, 554-1404).

(Sec. 4, Toxic Substances Control Act (TSCA), (90 Stat. 2006 (15 U.S.C. 2603)))

Dated: January 19, 1981.

Steven D. Jellinek,

Assistant Administrator for Pesticides and Toxic Substances.

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